

LISTING OF THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A method of diagnosis of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE), variant Creutzfeldt-Jakob Disease (vCJD), and Creutzfeldt-Jakob Disease (CJD) ~~or the possibility thereof~~ in a subject suspected of suffering from BSE, vCJD, or CJD, which comprises:

subjecting a sample of a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE-, vCJD-, or CJD- infected subjects and non- BSE-, vCJD-, or CJD- infected subjects, and is selected from the group consisting of:

(a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7500, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da; and

(b) cystatin C; and

~~(c) a hemoglobin, a hemoglobin chain, or a truncated chain or fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin;~~

comparing the test amount of the polypeptide in the sample to a reference amount of the same polypeptide contained in a sample of a body fluid selected from the group consisting of CSF, blood, plasma, and serum taken from a subject not infected with BSE, vCJD, or CJD, ~~wherein the reference amount of the polypeptide represents no BSE, vCJD, or CJD infection;~~ and

wherein an increase ~~or decrease~~ in the test amount of the polypeptide in the subject's body fluid of the subject suspected of suffering from BSE, vCJD, or CJD, compared to the reference amount of the polypeptide in the body fluid of the non-infected subject, indicates BSE, vCJD, or CJD in the subject suspected of suffering from BSE, vCJD, or CJD.

2. (Currently Amended) The method according to Claim 1, in which the polypeptide is present in the body fluid of BSE-, vCJD-, or CJD- infected subjects and not present in the body fluid of non- BSE-, vCJD-, or CJD-infected subjects, whereby the presence of the polypeptide in a body fluid sample in a subject suspected of suffering from BSE, vCJD, or CJD is indicative of BSE, vCJD, or CJD.

3. (Cancelled)

4. (Previously Presented) The method according to Claim 1, in which the mass spectrometry is laser desorption/ionization mass spectrometry.

5. (Currently Amended) The method according to Claim 4, in which the sample is adsorbed on a ~~probe~~ test strip or on a protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic or weak cationic exchange surface capable of binding the polypeptide.

6. (Previously Presented) The method according to Claim 4, in which the polypeptide is determined by surface-enhanced laser desorption/ionization (SELDI) and time of flight mass spectrometry (TOF-MS).

7. (Canceled)

8. (Previously Presented) The method according to Claim 1, in which a plurality of peptides is determined in the sample.

9. (Previously Presented) The method according to Claim 1, in which the TSE is Creutzfeldt-Jakob disease (CJD).

10. (Currently Amended) The method according to Claim 9, in which the TSE is sporadic Creutzfeldt-Jakob Disease (CJD) or variant Creutzfeldt-Jakob Disease (~~CJD~~ vCJD).

11. (Currently Amended) The method according to Claim 9, in which one or more polypeptides having a respective molecular weight of about 4780, about 6700, about 8600 or about 13375 Da is determined, and the presence of one or more of such polypeptides in a subject suspected of suffering from CJD is indicative of CJD.

12. (Cancelled)

13. (Currently Amended) The method according to Claim 9, in which a polypeptide having a molecular weight of about 7770 Da is determined, and the presence of such polypeptide in a subject suspected of suffering from CJD is indicative of CJD.

14. (Cancelled)

15. (Currently Amended) The method according to Claim 9, in which a polypeptide having a molecular weight of about 7574, about 7930, about 7975 or about 8020 Da is determined, and the presence or increased amount of one or more of such polypeptides in a subject suspected of suffering from CJD is indicative of CJD.

16. (Previously Presented) The method according to Claim 1, in which the TSE is Bovine Spongiform Encephalopathy (BSE).

17. (Currently Amended) The method according to Claim 16, in which the polypeptide has a molecular weight of about 10220 Da, and the presence of the polypeptide in a subject suspected of suffering from BSE is indicative of BSE.

18-28. (Cancelled)

29. (Currently Amended) A kit for diagnosis of a TSE selected from the group consisting of BSE, vCJD, and CJD, comprising:

a ~~probe test strip~~ or protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic, or weak cationic exchange surface capable of binding a polypeptide onto which a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma, and serum is adsorbed, and for placement in a mass spectrometer, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE-, vCJD-, or CJD- infected subjects and non- BSE-, vCJD-, or CJD- infected subjects, and is selected from the group consisting of:

(a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7500, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da; and

(b) cystatin C; and

~~(c) a hemoglobin, a hemoglobin chain, or a truncated chain or fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin;~~

wherein diagnosis of TSE BSE, vCJD, or CJD is determined by comparing the test amount of polypeptide to a reference amount of the same polypeptide, wherein a significant increase in the test amount of the polypeptide in the body fluid of the subject suspected of suffering from BSE, vCJD, or CJD, compared to the reference amount of polypeptide represents that the subject is suspected of suffering from ~~ne~~ BSE, vCJD, or CJD infection.

30. (Currently Amended) The kit according to Claim 29, in which the ~~probe test strip~~ contains an adsorbent for adsorption of the polypeptide.

31. (Currently Amended) The kit according to Claim 29, further comprising a washing solution for removal of unbound or weakly bound materials from the ~~probe test strip~~.

32-47. (Cancelled)

48. (New) A method of diagnosis of a transmissible spongiform-encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE), variant Creutzfeldt-Jakob Disease (vCJD), and Creutzfeldt-Jakob Disease (CJD) in a subject suspected of suffering from BSE, vCJD, or CJD, which comprises:

subjecting a sample of a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE-, vCJD-, or CJD- infected subjects and non- BSE-, vCJD-, or CJD- infected subjects, and is selected from the group consisting of:

- (a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7500, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da; and
- (b) cystatin C; and

comparing the test amount of the polypeptide in the sample to a reference amount of the same polypeptide contained in a sample of a body fluid selected from the group consisting of CSF, blood, plasma, and serum taken from a subject not infected with BSE, vCJD, or CJD; and

wherein a decrease in the test amount of the polypeptide in the body fluid of the subject suspected of suffering from BSE, vCJD, or CJD, compared to the reference amount of the polypeptide in the body fluid of the non-infected subject, indicates BSE, vCJD, or CJD in the subject suspected of suffering from BSE, vCJD, or CJD.

49. (New) The method according to Claim 48, in which the polypeptide is not present in the body fluid of BSE-, vCJD-, or CJD- infected subjects and present in the body fluid of non-BSE-, vCJD-, or CJD-infected subjects, whereby the non-presence of the polypeptide in a body fluid sample is indicative of BSE, vCJD, or CJD.

50. (New) The method according to Claim 48, in which the mass spectrometry is laser desorption/ionization mass spectrometry.

51. (New) The method according to Claim 50, in which the sample is adsorbed on a test strip or on a protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic or weak cationic exchange surface capable of binding the polypeptide.

52. (New) The method according to Claim 50, in which the polypeptide is determined by surface-enhanced laser desorption/ionization (SELDI) and time of flight mass spectrometry (TOF-MS).

53. (New) The method according to Claim 48, in which a plurality of peptides is determined in the sample.

54. (New) The method according to Claim 48, in which the TSE is Creutzfeldt-Jakob disease (CJD).

55. (New) The method according to Claim 54, in which the TSE is sporadic Creutzfeldt-Jakob Disease (CJD) or variant Creutzfeldt-Jakob Disease (vCJD).

56. (New) The method according to Claim 54 in which one or more polypeptides having a respective molecular weight of about 3970, about 3990, about 4294, about 4478, about 10075, about 11730, about 14043 or about 17839 Da is determined, and the absence of one or more of such polypeptides in a subject suspected of suffering from vCJD or CJD is indicative of vCJD or CJD.

57. (New) The method according to Claim 54, in which a polypeptide having a molecular weight of about 3295, about 4315, about 4436, about 6200, about 8936, about 9107, about 9145, about 9185, about 9454 or about 13550 Da is determined, and the absence or decreased amount of one or more of such polypeptides in a subject suspected of suffering from vCJD or CJD is indicative of vCJD or CJD.

58. (New) The method according to Claim 48, in which the TSE is Bovine Spongiform Encephalopathy (BSE).

59. (New) A kit for diagnosis of a TSE selected from the group consisting of BSE, vCJD, and CJD, comprising:

a test strip or protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic, or weak cationic exchange surface capable of binding a polypeptide onto which a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma, and serum is adsorbed, and for placement in a mass spectrometer, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE-, vCJD-, or CJD- infected subjects and non-BSE-, vCJD-, or CJD- infected subjects, and is selected from the group consisting of:

- (a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7500, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da; and
- (b) cystatin C; and

wherein diagnosis of TSE is determined by comparing the test amount of polypeptide to a reference amount of the same polypeptide, wherein a significant decrease in the test amount of the polypeptide in the body fluid of the subject suspected of suffering from BSE, vCJD, or CJD, compared to the reference amount of polypeptide represents that the subject is suspected of suffering from BSE, vCJD, or CJD infection.

60. (New) The kit according to Claim 59, in which the test strip contains an adsorbent for adsorption of the polypeptide.

61. (New) The kit according to Claim 59, further comprising a washing solution for removal of unbound or weakly bound materials from the test strip.